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ORIGINAL PAPER

Psychopharmacological Enhancement

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Abstract Many drugs have therapeutic off-label uses for which they were not originally designed. Some drugs designed to treat neuropsychiatric and other disorders may enhance certain normal cognitive and affective functions. Because the long-term effects of cognitive and affective enhancement are not known and may be harmful, a precautionary principle limiting its use seems warranted. As an expression of autonomy, though, competent individuals should be permitted to take cognition- and mood-enhancing agents. But they need to be aware of the risks in chronic use of these agents and to take responsibility for their effects. A reasonable middle ground between these positions is to warn those who choose to enhance that doing so entails risks.

Keywords Authenticity · Anxiety · Attention · Memory · Methylphenidate · Modafinil · Propranolol

Introduction

Many drugs have therapeutic off-label uses for which they were not originally intended. These uses were not part of the approval of the drugs and are not included in their labelling. Some drugs designed to

treat neuropsychiatric disorders can enhance certain normal cognitive functions. Methylphenidate (Ritalin) can help people with ADHD to focus attention and carry out cognitive tasks. This same drug might also help university students and others who do not have this disorder to increase their concentration and perform better on exams or in their work. Modafinil (Provigil) has been prescribed for narcolepsy, sleep apnea, and shift-work sleep disorder. Now it is used to promote alertness in people with regular sleep–wake cycles. Other drugs are being designed to enhance the consolidation, storage, and retrieval of memory for people without any memory impairment. SSRIs (selective serotonin reuptake inhibitors) such as fluoxetine (Prozac) are prescribed for the treatment of depression and anxiety disorders. Yet some who have not been diagnosed with these disorders take these drugs to enhance their mood and feel “better than well” [10, 17].

Some philosophers and bioethicists are concerned that the use of these and other drugs to enhance normal cognition and mood would result in a state of inauthenticity [10, 24]. The drugs would create states of mind that would in some sense be alien to people taking them. I will show that this concern about authenticity is unfounded. Then I will discuss what I believe are more ethically significant questions about the safety of enhancement drugs and consider the potential benefits and risks of using them for this purpose. In addition, I will argue that universal access to cognition-enhancing agents would not help to reduce social inequality, but also that unequal access

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to these drugs would not necessarily be unfair to those who could not afford them. I will consider some of the possible consequences of employers encouraging employees to use these drugs in order to enhance productivity. Finally, I will address the question of whether cognitive enhancement would fundamentally alter the doctor–patient relationship. Because the long-term effects of cognitive and affective enhancement are not known and could be harmful, a precautionary principle may be warranted. Safety concerns seem to justify limiting its use. As an expression of autonomy, though, competent individuals should be permitted to take enhancing agents. But they need to be aware of the risks in chronic use of these agents and to take responsibility for their effects. A reasonable middle ground between these positions is to warn those who choose to enhance that doing so entails risks.

Alienation? Inauthenticity?

One concern about enhancing normal cognitive capacities with drugs is that it would result in alienation from our true selves. Our selves consist partly in a unified set of psychological properties that are generated and sustained by normally functioning processes in the brain and central nervous system. We come to have authentic selves by identifying with our mental states. The state of identification results from a process of critical reflection on our desires, beliefs, intentions and other states of mind. It is through this reflection that we reinforce or reject them as the springs of our actions. Having an authentic self consists in having the higher-order reflective capacity to control which motivational states issue in our actions [14, 15, 23]. This capacity is a necessary condition for authentic and responsible agency, and insofar as agency is an essential component of selfhood, being an authentic agent is part of being an authentic self. Altering the process of critical reflection and the motivational states that result from it with psychotropic drugs presumably would result in alienation of our true selves from these states. We could not identify with these altered states and could not have authentic selves because something alien to us would be the agent of the change.

But it is not obvious that any drugs used to enhance cognition or mood would make our selves

inauthentic. If an individual with the capacity for practical reasoning freely decides to take a cognition- or mood-enhancing agent, then he or she is the agent of change. The drug is merely the means through which the change in mental states is effected. Provided that the individual has the capacity to critically reflect on the reasons for and against enhancement and to voluntarily act on these reasons, the change in mental states would not necessarily result in an alien or inauthentic self. The individual would have the capacity to foresee the change in mental states, and insofar as this is what he or she desires, intends, and decides to do after critical reflection, the change would be of his or her own doing. The realization of the intention to alter some of one's mental states would not necessarily alter numerical identity. Despite the changes, one could remain the same person after taking the drug, though it would depend on how substantial the changes were. The alteration could also be consistent with one's narrative identity. It could be an essential part of the unified set of values and interests over the course of one's entire biographical life. [8, 26].

Even if one claimed that any psychological discontinuity between the earlier and later mental states would be substantial enough to result in distinct selves, the capacity to foresee the consequences of enhancement would be enough to make one responsible for them. Consider Stevenson's tale of Dr. Jekyll and Mr. Hyde. Jekyll transforms himself into the evil Hyde by voluntarily taking a potion. Later, when his curiosity moves him to repeat the experiment, he finds himself the subject of the involuntary mental states that characterize Hyde. Although it is Hyde who commits the evil deeds, Jekyll is responsible for them because he has the capacity to know that they are the likely consequences of his experiment and to prevent them by not taking the potion in the first place. Foreseeability makes the responsibility transfer from the earlier to the later time. This seems to be the point of Jekyll's admission, when speaking of Hyde, that "this too was myself" ([30], 133).

Attention and Alertness

Methylphenidate is a central nervous system stimulant and dopamine reuptake inhibitor. When used as a form of enhancement, it can increase attention in

people whose dopamine levels are normal. Yet in brains with normal levels of dopamine, methylphenidate may cause dopamine dysregulation in various neural networks and lead to cognitive and conative abnormalities such as addiction. This has occurred, for example, in some patients taking dopamine agonists for Parkinson's disease [9]. The drugs overcompensated for the dopamine depletion in the basal ganglia and other regions implicated in the disease.

Experiments using modafinil have shown that it can keep people alert and engaged in mental activities despite long periods of sleep deprivation [32, 33]. It is believed that this drug activates dopamine, which then activates norepinephrine and histamine in a process that blocks the hypothalamus from promoting sleep. Modafinil does not appear to produce the same hyperactive and addictive effects of stimulants like amphetamines and cocaine because of its selectivity in targeting the dopamine pathway that controls wakefulness.

If the use of modafinil resulted in long-term REM sleep deprivation, however, then it could have deleterious effects on the brain and body [27, 28]. Constant release of monoamines such as serotonin to sustain prolonged awareness of the environment may desensitize neurotransmitter receptors. REM sleep appears to inhibit monoamine release and allow the receptors to rest and reset themselves and retain sensitivity. Disturbing this process may have adverse effects of cognition and mood. In addition, non-rapid-eye-movement (NREM) sleep provides a period of low metabolic demand in the brain, which allows neuronal energy resources to be replenished. This is necessary for the brain to meet high metabolic demand during wakefulness. Drugs such as modafinil that limited NREM sleep could disrupt brain metabolism and interfere with the brain's ability to support cognitive tasks. Sleep also plays an important role in maintaining neural plasticity. Limiting sleep through pharmacological means could impair the brain's ability to adapt to changing environments or to adjust to injury. People who are chronically sleep-deprived (4 h or less per night) generally are at greater risk of morbidity and mortality than those who sleep 6 to 8 h per night. The shorter sleepers have a higher incidence of cardiovascular problems such as hypertension and neurological problems such as stroke and are more susceptible to infection because of weakened

immune systems. Sleep deprivation may also be a risk factor for metabolic and endocrine disorders such as obesity and diabetes. Chronic use of a drug like modafinil might cause or exacerbate these conditions.

There are established contraindications for modafinil. It should be used with caution in patients with a history of psychosis or cardiovascular disease. Its side effects are similar to those of other stimulants. More precisely, some individuals taking this drug experience confusion, ataxia, hyperglycemia, paresthesia, dyspnea, and other symptoms [29]. In principle, a competent individual should be permitted to take modafinil to enhance alertness if he or she so desires. But one's prudential reasons for taking it should include awareness of these contraindications and a careful weighing of its potential benefits and risks.

Memory

Research into the mechanisms of memory suggests that novel pharmacological agents could enhance the encoding and storage of episodic and semantic memory of events and facts. "Smart" drugs targeting the transcription factor cyclic AMP response element binding protein (CREB), which influences the encoding and storage of long-term memory, might increase memory capacity in our brains. [20, 31] This effect might also be achieved through drugs that increased levels of acetylcholine, the main neurotransmitter involved in the regulation of memory. Other pharmacological agents that might have a similar effect are ampakines, which can influence the neurotransmitter glutamate and promote better communication between synapses in the cortex. These agents might also enhance the retrieval of remembered facts and events from the hippocampus and other sites in the medial temporal lobes by the prefrontal cortex for short-term working memory in executive cognitive functions. Insofar as it would be used by people with normal memory functions, enhancement would be different from the therapeutic use of drugs such as the cholinesterase inhibitor donepezil (Aricept) and the glutamate antagonist memantine (Namenda) to retard memory loss in Alzheimer disease. Memory enhancement could result in more effective cognitive capacities such as problem-solving and decision-making. Would these drugs enable us to form and store more memories and retrieve them more quickly? Or would

increasing the storage capacity of memories impair our capacity to retrieve them?

These questions are motivated by an evolutionary interpretation of memory. The limits we have in our normal capacity to remember only so many facts and so many events may be part of an adaptive mechanism that is critical to our survival. In that case, attempting to increase the storage capacity in one system could have adverse effects on formation or retrieval in that same system. It could also have adverse effects on formation, storage, and retrieval mechanisms in other memory systems.

The idea that there is an adaptive limit to memory formation and storage is based on the hypothesis that there is a balance between two types of CREB in the brain: “activator CREB; and “blocker” CREB [1]. The first type activates the genes and gene products necessary for the encoding or formation of long-term memory, while the second type inhibits the formation of additional long-term memory. Blocker CREB may also remove existing memories from storage sites in the hippocampus and cortex if the brain deems them to be unnecessary. It does this in order to prevent mental “noise” that would interfere with our ability to concentrate on immediate mental activities and to anticipate the future. Too much blocker CREB could result in forgetfulness and, in severe cases, dementia. Too much activator CREB could result in an overproduction and oversupply of memory, the brain and mind being cluttered with memories of facts and events that served no purpose. Drugs designed to enhance memory would aim to increase the amount of activator CREB. But if there is an adaptive balance between the two types of CREB, and between remembering and forgetting, then drugs that increased memory storage could upset this balance. One possible consequence of this might be impaired memory retrieval. Neuroscientist Martha Farah expresses this same concern: “We understand very little about the design constraints that were being satisfied in the process of creating a human brain. Therefore we do not know which ‘limitations’ are there for a good reason... Normal forgetting rates seem to be optimal for information retrieval” ([11], 1125).

Another possible consequence of increased memory would be difficulty in learning new things, which depends on a certain degree of forgetting. The most famous case of this condition was the patient

Shereshevskii, as reported by the neuropsychologist A. R. Luria [19]. Shereshevskii’s formidable ability to remember facts and events resulted in his inability to process new information. The only employment he could sustain was that of a travelling mnemonist. A fictional illustration of this condition is the character Ireneo Funes in Jorge Luis Borges’ story “Funes the Memorious” [2]. Funes sustains a brain injury from an equestrian accident. Consistent with Borges’ penchant for irony, Funes does not develop amnesia but instead a condition in which he remembers every detail of everything he experiences. Speaking to the narrator, Funes says, “My memory, sir, is like a garbage disposal” (p. 32). He becomes an invalid, a prisoner of a hyperactive system of memory consolidation and recall, unable to learn new things and anticipate the future because he cannot tolerate any additional experience. The narrator suspects that Funes “was not very capable of thought. To think is to forget a difference, to generalize, to abstract. In the overly replete world of Funes, there were nothing but details, almost contiguous details” (p. 36). Because of his overloaded memory, Funes is unable to execute such cognitive tasks as problem-solving and decision-making. He is also unable to anticipate and plan for the future because he cannot forget the particular features of his experience. Borges writes that Funes died from “pulmonary congestion” (p. 36), which could be taken as a metaphor for his overloaded memory.

The problems of memory overload that I have described could be avoided by separating retrieval of recent memories from retrieval of remote memory. In theory, drugs could be designed to avoid any adverse effects by enhancing the storage and retrieval of recent memory while allowing normal forgetting rates of remote memory. Perhaps drugs targeting mechanisms regulating working memory could have this effect. But even recent memory can include many trivial details that can clutter the mind. It is unclear how specially designed drugs could weed out recent memory of trivial facts from recent memory of useful facts, or whether quicker retrieval would not have any untoward effects on memory formation and storage. There are other critical features of memory consisting of more than mechanisms of encoding, storage, and retrieval. It is unclear what effects drugs designed to enhance these mechanisms might have on these other features of our ability to recall the past. It is possible

that the drugs might do more to impair than improve the usefulness and value of memory.

A recent study by Hassabis et al. sheds some light on the problem exemplified by Luria's patient and Borges' fictional character. The Hassabis study compared people with bilateral hippocampal amnesia with people whose episodic memory was intact. Whatever episodic memory the amnesiacs retained consisted mainly in recalling trivial details of past events. They were unable to express the general meaning of these events and unable to imagine new experiences. This supports the hypothesis that remembering the past and imagining the future are interrelated mental capacities. Unlike the amnesiacs, Shereshevskii and Funes had a preternatural capacity for recall. Yet the fact that none of these individuals was able to capture the gist of the past suggests that what matters is not just *how much* one can recall, but also *how* one recalls it. The ability to meaningfully recall the past and anticipate the future appears to depend as much on qualitative as on quantitative aspects of our episodic memory. Hassabis' study suggests that increasing the quantity of memory might interfere with the qualitative capacity to make sense of past experience and simulate future experience. Among other things, this dual constructive capacity enables us to have a unified set of psychological properties necessary for our experience of ourselves as subjects persisting through time. While this requires a certain amount of memory storage and retrieval, it is more than a function of how many memories of specific details our brains can store, or of how efficiently our brains can retrieve them for cognitive tasks.

As Daniel Schacter and Donna Rose Addis point out, "remembering the gist of what happened is an economical way of storing the most important aspects of our experiences without cluttering memory with trivial details" ([25], 27). They also note that "information about the past is useful only to the extent that it allows us to anticipate what may happen in the future" ([25], 27). The extent to which we can learn new things is a function of the meaning we can construct from our past experience ([16], 1726). Memory is not just a reproduction of past events. The brain and mind do not function as a video recorder, or as a bank from which we withdraw particular memories of facts and events stored in specific sites in the brain. In addition to the

hippocampus in the temporal lobe, regions in the frontal and parietal lobes play a role in the dual capacity to remember the past and anticipate the future. The parietal lobe, which regulates our orientation to space and time, is critical for this capacity. Together with the hippocampus, it provides a holistic representation of the environmental setting in which we can meaningfully recall past experience and simulate or imagine future experience. These brain regions and the capacities they mediate are critical not only to our experience of persisting through time. They are also critical to the capacity of a human organism to make sense of its interactions with the social and natural environment.

Memory researcher James McGaugh insists that we should be wary of inferring that if a certain amount of memory is good, then more memory is better [21, 22]. Our capacity to form and store more memories might leave us too focused on the past, which might alter our phenomenological experience of persisting from the past to the future. Our cognitive capacities could be diminished by our ability to recall more facts and events that had little or no meaning or purpose for us. Before we pharmacologically tinker with memory systems, we need to consider how this might affect our neurological and mental capacities that mediate the content and meaning of memory. We should look to Luria's patient Shereshevskii, Borges' character Funes, and the individuals in Hassabis' study with bilateral hippocampal amnesia as examples of the consequences we would want to avoid.

Keeping One's Cool

Anxiolytics are prescribed and taken for conditions falling within generalized anxiety disorder (GAD). These drugs include benzodiazepines such as diazepam (Valium) and lorazepam (Ativan), which block the release of stress hormones such as adrenaline. Yet these drugs are now being used by people who do not have GAD in order to remain calm when they have to act or interact with others in public. The beta-adrenergic antagonist propranolol (Inderal) is primarily an antihypertensive and antiarrhythmic drug designed to reduce the cardiovascular excitatory response to adrenaline and norepinephrine. By reducing this response in the brain as well, propranolol can attenuate or prevent anxiety. Some musicians and

public speakers may take propranolol to block the stress response and thereby enhance their musical or oratorical performance in recitals, concerts, and lectures.

One musician taking propranolol told me that, while his performances seemed to improve, the lack of an “adrenaline rush” blunted the normal experiential “feel” of these performances for him. He also noted that he had only a vague memory of some of his performances. This can be explained by the role of stress hormones in memory consolidation. Adrenaline and norepinephrine are necessary for the encoding and consolidation of emotional memories in the amygdala. They also may be necessary for the encoding and consolidation of episodic memories in the hippocampus. This might explain why some people taking benzodiazepines experience some degree of anterograde amnesia, or impairment in their ability to form new memories. An anti-anxiety drug may enable one to keep one’s cool during a performance, only to block the memory of that performance. Moreover, it is not known what effects the continued use of a drug that blocked a natural hormonal response might have on systems other than the cardiovascular and central nervous systems.

Blocking natural hormonal responses to our interactions with others in the social environment might also interfere with our emotional responses to these interactions. Any benefits of these drugs in enhancing cognitive capacities may come at the cost of becoming disengaged from one’s emotions. It is also possible that, given the connection between cognition and emotion, a pharmacological agent overactivating the first faculty and underactivating the second could impair reasoning and decision-making [6, 7]. This would depend on the extent to which a beta-adrenergic antagonist such as propranolol affected cognition ([18], 193). The constellation of psychological properties resulting from cognitive enhancement might not be so desirable in every case.

Suppose that a 10-year-old female is a piano prodigy. Her parents and teachers believe that she is destined for greatness in the musical world. But she becomes anxious before her public performances. To prevent anxiety, her parents give her propranolol, which calms her and ensures a flawless musical performance in every instance. Encouraged by her parents, the child identifies with her musical prowess and desires to be a world-class musician. It appears

that the child’s ability to perform at the highest level will be an essential component of her well-being over the course of her life. Would there be anything objectionable about using propranolol in this case?

The fact that the pianist is not a mature minor or adult and does not have the decisional capacity to carefully think through the benefits and risks of chronic use of propranolol is significant. She, not her parents, would experience any long-term adverse effects of the drug. Because she does not have decisional capacity, and because the drug may involve some risk to her health, one could object to the parents’ decision to allow her to take propranolol. It is not obvious that chronic use of this drug would be in her long-term best interests. This is a decision she could make on her own once she is competent enough to weigh the benefits and risks of the drug. The objection to permitting her parents to make decisions about propranolol for her can be sustained despite the fact that the drug appears to enhance her musical development, and that discontinuing the drug may foreclose future opportunities for her. It is possible that, by the time she is mature enough to make critical decisions, she may no longer identify with the desire to be world-class musician. Even if the possibility of being a great musician were lost, she might be able to accommodate her interests to different possibilities or develop new interests. By insisting that their daughter take propranolol, the parents may be interfering with her right to an open future, which will only begin to take shape once she is capable of making her own decisions [13]. Only in cases where anxiety significantly limits a child’s ability to function in everyday life would parental consent to the child’s use of propranolol or any anxiolytic be justified. In these cases, anxiolytics would be justified for therapeutic uses, but not for enhancement.

Some mature adolescents or adults may take an SSRI instead of an anxiolytic for a similar purpose. Shyness may underlie their anxiety, and they may believe that an antidepressant may enable them to overcome this condition and become more successful in all of their projects. There are questions about just how effective these agents are for this purpose. Farah has noted that “the small literature on short-term SSRI effects in normal subjects suggests no change in either direction on positive affect, only a selective decrease in negative affect” ([11], 1125). However, there are potentially serious side effects of SSRIs in people

with normal levels of serotonin, norepinephrine, and dopamine. Because antidepressants can increase the availability of these neurotransmitters, they may result in hypomania or mania in some biologically vulnerable people. Hypomania can be confused with a cheerful disposition, and taking drugs to enhance mood could unwittingly cause this mental disorder. In addition, these drugs may trigger the serotonin syndrome, which is usually caused by a combination of two or more drugs, one of which is an SSRI. It is a consequence of excess serotonin in the central nervous system. The syndrome's symptoms can include euphoria, drowsiness, exaggerated reflexes, hyperthermia, and in some cases, coma and death. The serotonin syndrome occurs in approximately 14 to 16% of persons who overdose on SSRIs [3]. In a well-known case in a New York Hospital in 1984, a combination of meperidine (Demerol) and phenelzine (Nardil) resulted in this syndrome and the death of 18-year-old Libby Zion.

It is not known what the long-term cognitive, affective, or conative effects of drugs to enhance alertness, memory, or public performance might be. What *is* known is that most drugs have side effects. Admittedly, this concern is not unique to enhancement drugs but applies to therapeutic drugs as well. Still, it is one thing to administer a drug with potential adverse effects for therapeutic treatment of a mental disorder. It is quite another thing to administer a drug with potential adverse effects to enhance normal mental functions. This raises the question of why one would take the risk of experiencing adverse effects of a drug if there is no medical need for it. Until there is a better understanding of the risks of drugs intended for cognitive enhancement, the potential harm from long-term use of these drugs suggests that they should be limited to short-term use in special circumstances and only when there is a compelling reason to use them. Yet because the long-term effects of enhancement are not yet known, it would be difficult to advocate for a policy that prohibited their use for this purpose. It should be up to individuals to choose whether to take cognition- or mood-enhancing drugs, provided that they are warned of the risks.

Some may question the selective concern about the drugs I have discussed. Many people take certain foods or supplements to improve cognitive and affective states of mind. Why is there such concern about drugs when food and supplements are taken to

produce the same effects? Others may question why some drugs but not others concern us. Why do we not worry as much about the effects of nicotine or alcohol as we do about the effects of modafinil, CREB enhancers, anxiolytics, or SSRIs to enhance cognition or mood?

The effects of psychotropic drugs on the brain and central nervous system are more immediate and profound than the effects of foods and supplements. The fact that a comparatively lower dose of an SSRI has a much greater effect on brain biochemistry and mood than higher doses of St. John's wort or tryptophan indicates a significant difference in their effects on the brain. Similarly, modafinil and other stimulants such as dextroamphetamine have more pronounced effects on brain biochemistry and alertness than caffeine. The difference between pharmacological agents and foods or supplements in their effects on the brain and central nervous system may be one of degree rather than kind. But the difference of degree is significant, which gives us a reason to be concerned about the chronic use of these agents. Regarding the second question, we should indeed be just as concerned about nicotine and alcohol as we are about psychotropic drugs. The adverse effects of nicotine and alcohol on the brain and body are just as harmful to individuals as the adverse effects of psychotropic drugs. Accordingly, all of these substances should be discussed in the same context of the risks to those who use them.

Social Issues

Attention, memory, and other cognitive capacities are all components of intelligence, which is a competitive good. It can give some people a competitive advantage over others in gaining employment, income, wealth, and a higher level of well-being. This advantage, and the social inequality that results from it, might be perceived as unfair because intelligence is a set of capacities that one has or lacks through no merit or fault of one's own.

Some have argued that the best way to ameliorate this situation would be to offer cognitive enhancement drugs to all. Ideally, it would give everyone an equal opportunity for access to the type of education and employment that would guarantee a moderate to high level of well-being for everyone. Farah has cited

research indicating that any positive effects of enhancement drugs are more modest in people with higher levels of cognitive function and greater in people with lower levels of cognitive function [11, 12]. This might suggest that cognition-enhancing drugs could do much to reduce inequality in intelligence and access to other competitive goods. But this would not necessarily follow. Equal access to these drugs would not imply equal opportunity or equal outcomes from using them.

Different parental attitudes to related competitive goods such as an elite education and lucrative jobs could mean substantial differences among children in the extent to which enhancing agents were utilized. Some parents would be more selective than others in sending their children to better schools or in arranging for private tutors. In these respects, equal access to cognitive enhancement would not automatically result in equal opportunity for academic achievement among children. Moreover, some adolescents and adults would use cognition-enhancing drugs for trivial activities. Instead of using methylphenidate to enhance alertness or other drugs to enhance memory in order to perform better on the SAT or university exams, some people would use these drugs to memorize phone numbers or sports statistics. Or they might use them for pathological pursuits such as gambling. Not everyone would use these drugs in a beneficial way. So there would be unequal outcomes of cognitive enhancement with respect to the competitive goods at issue. Any beneficial options of enhancement would likely come on top of existing social inequality. It would more likely maintain or increase than reduce inequality in whether or to what extent people gained competitive goods.

Universal access to drugs intended to enhance cognition is not a likely scenario. States would be reluctant to take on what would be an exorbitant cost. Access to these expensive drugs would be based instead on the ability to pay for them. Because some people are financially worse off than others through no fault of their own, this would seem unfair to those who could not afford to pay for the drugs. They would not have the same access to the drugs as those who were financially better off. But any claim of unfairness would have to be supported by a significant body of data on the long-term benefits and risks of the drugs. The relevant data are not currently

available. If the benefits and risks of these agents were not known, then there would be no basis on which to claim that unequal access to the drugs would be unfair to those who could not afford them. The claim about unfair access rests on the questionable assumption that the drugs would have only beneficial outcomes. Yet it is possible that those who used the drugs over time might experience more harmful than beneficial effects. They could end up being worse off in terms of their physical and mental health than those who could not purchase the drugs. Inequality in access to cognition-enhancing drugs between the financially better off and worse off would not necessarily be unfair to the latter.

Employers might pressure employees to use cognition-enhancing agents such as modafinil or methylphenidate to execute cognitive tasks over a longer period and thereby increase productivity. Some employees might decline to use them, either because of concern about their safety or a more general concern about deleterious effects of longer hours and increased productivity on their health. If the drugs were effective, then those who declined to use them could be at a competitive disadvantage compared with their colleagues who used them [5, 12]. This could jeopardize their jobs. Yet this assumes that the drugs would have only salutary effects on the brain and body. This may be true for short-term use; but it cannot be assumed that longer-term use would have only salutary effects. If chronic use of the drugs resulted in adverse effects, then it is not clear that the employees who used them, or the employer who encouraged their use, would be any better off. Adverse effects of the drugs could result in disability claims by employees, which would result in negative financial and legal consequences for the employer.

There is another reason for questioning claims about fairness in access to cognition-enhancing drugs. Leaving safety issues aside, it is not clear that these drugs would have the same beneficial effects for everyone who took them. Given differences in people's brains and their varying responses to psychotropic drugs, it is possible that some people would derive only a modest benefit from taking them, or no benefit at all. One cannot assume that just because these drugs may have positive effects on the brains of some people, they would have positive effects on the brains of all people.

Implications for the Doctor–Patient Relationship

Suppose that cognition- and mood-enhancing drugs were proven to be safe as well as effective. But they would not be available over the counter or the Internet. Suppose further that a person wanted a drug to enhance his or her cognitive functions or mood and asked a doctor to prescribe it for him or her. Assuming that the drug was safe, there would be no risk of harm to the individual, and the doctor would be permitted to prescribe it. But there would be no therapeutic relationship between doctor and patient, given that the individual in such a case would not have a disease or illness in any sense of these terms. Even if we construe “therapy” loosely, it is unclear how an intervention that did not restore a patient to, or maintain a patient at, a normal level of mental and physical functioning could be described as therapeutic. The relationship in the case imagined here would not be therapeutic, since there would be no condition justifying medical intervention for treatment or prevention. Thus the doctor would have no duty of beneficence and no obligation to prescribe the drug simply because the individual wanted it.

Modafinil may be prescribed as an alternative to methylphenidate for the treatment of ADHD. Given that ADHD is a psychiatric disorder, this use of the drug would clearly be therapeutic. There may also be compelling reasons for prescribing modafinil for people who need it to perform specific occupational tasks. Airline pilots on transcontinental flights and night-shift workers would fall within this group. Whether the use of a drug is described as a form of therapy or enhancement depends not on the drug itself but the purpose of its use. Doctors are obligated to treat neurological, psychiatric, and other diseases and thereby alleviate pain and suffering in patients who have these diseases. This often involves prescribing certain medications. In cases like the two just mentioned, doctors may prescribe medications necessary for certain types of work. But they are not obligated to make people more competitive or happy.

Some have speculated that the possibility of neurocognitive enhancement could fundamentally alter the doctor–patient relationship [4, 5, 12]. Whether it does this will depend on physicians’ views on what it means to have a therapeutic relationship with patients, whether this is a fiduciary relationship,

and what it means to act in patients’ best interests. It will depend on how physicians conceive of and exercise their professional autonomy in discharging their duty of care to patients. There may be considerable variation among physicians in how they exercise this autonomy, which would reflect their views on which psychopharmacological interventions they considered to be therapy, and which they considered to be enhancement.

Conclusion

The human nervous system is much more complex and sensitive to stimuli than any other system in the human body. For this reason, and because the brain regulates our thought and behaviour, the potential harm from chronic pharmacological intervention in the brain must be taken seriously. The plasticity of the brain and the neurological and psychological effects from manipulating it also distinguish cognitive and mood enhancement from other forms of bodily enhancement, such as cosmetic surgery. If chronic use of psychotropic drugs to enhance mental functions entailed only minimal benefit and a significant risk of harm, and they were not medically indicated to treat a disease, then there would be no good medical or ethical reasons for doctors to prescribe them to patients. Indeed, they might be prohibited from doing this on grounds of nonmaleficence. Even if drugs that enhanced cognition and mood were effective and safe, doctors would not be obligated to prescribe them to people for these off-label purposes just because they wanted them. In addition, these drugs would more likely maintain or increase than reduce social inequality. Equal access to these drugs would not ensure equal beneficial outcomes.

A significant body of data on the long-term effects of psychopharmacology to enhance normal levels of cognition or mood is not yet available. So there is no decisive reason for a policy that would prohibit the use of drugs for this purpose. Nevertheless, the potential harm from chronic use of enhancing drugs could be significant, which would seem to justify erring on the side of safety and adopting a precautionary principle limiting their use. At the same time, as an expression of autonomy competent individuals should be permitted to take enhancing drugs and to

take responsibility for their effects. In adopting a reasonable middle ground between these two positions, we should issue the warning: "User Beware."

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